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Effectiveness of Azelastine Nasal Spray Compared with Oral Cetirizine in Patients with Seasonal Allergic Rhinitis

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ABSTRACT

Background: Azelastine nasal spray and oral cetirizine are selective histamine H_1-receptor antagonists that are approved in the United States for the treatment of seasonal allergic rhinitis (SAR).

Objective: The objective of the present study was to compare the efficacy and tolerability of azelastine nasal spray administered at the recommended dosage of 2 sprays per nostril twice daily with those of cetirizine in the treatment of moderate to severe SAR.

Methods: This multicenter, randomized, double-blind, parallel-group, 2-week comparative study was conducted during the 2004 fall allergy season in patients with moderate to severe SAR. After a 1-week placebo lead-in period, patients were randomized to receive azelastine nasal spray 2 sprays per nostril twice daily plus placebo tablets or cetirizine 10-mg tablets once daily plus a placebo saline nasal spray for the 2-week double-blind treatment period. The primary efficacy variables were (1) change from baseline to day 14 in the 12-hour reflective total nasal symptom score (TNSS), which combines scores for rhinorrhea, sneezing, itchy nose, and nasal congestion, and (2) onset of action, based on the instantaneous TNSS over 4 hours after the first dose of study drug. During the double-blind treatment period, patients recorded their symptom scores on diary cards twice daily (morning and evening). Patients aged ≥18 years also completed the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) at baseline and on day 14.

Results: Three hundred seven patients were randomized to treatment, and 299 completed 2 weeks of study treatment. The age of the population ranged from 12 to 74 years (mean, 35 years), 62.9% were female, and 69.6% were white. Over 2 weeks of treatment, both groups had significant improvements in the TNSS compared with baseline ($P < 0.001$). The overall change in TNSS was significantly greater with azelastine nasal spray compared with cetirizine (29.3% vs 23.0% improvement, respectively; $P = 0.015$). In terms of onset of action, azelastine nasal spray significantly improved the instantaneous TNSS compared with cetirizine at 60 and 240 minutes after the initial dose (both, $P = 0.040$). Scores on each domain of the RQLQ were significantly improved in both groups compared with baseline ($P < 0.001$); the overall RQLQ score was significantly improved with azelastine nasal spray compared with cetirizine ($P = 0.049$). Both treatments were well tolerated.

Conclusion: In this 2-week study in patients with moderate to severe SAR, azelastine nasal spray was well tolerated and produced significantly greater improvements in TNSS and total RQLQ score compared with cetirizine. (*Clin Ther.* 2005;27:543–553) Copyright © 2005 Excerpta Medica, Inc.

Key words: azelastine nasal spray, cetirizine, allergic rhinitis, double-blind clinical trial.

INTRODUCTION

Azelastine nasal spray† is a topical second-generation antihistamine indicated for the treatment of seasonal

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†Trademark: Astelin® (MedPointe Pharmaceuticals, Somerset, New Jersey).

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allergic rhinitis (SAR) and nonallergic vasomotor rhinitis. The active ingredient, azelastine hydrochloride, is a high-affinity histamine H_1-receptor antagonist with potency at the H_1-receptor site ~10 times greater than that of chlorpheniramine.[1] In addition to histamine antagonism, azelastine has been shown in clinical studies to have inhibitory effects on leukotrienes,[2] bradykinin and substance P,[2,3] cytokines,[4] intercellular adhesion molecule–1 (ICAM-1) expression,[5] and eosinophil chemotaxis.[5] Cetirizine hydrochloride* is an oral second-generation antihistamine indicated for the treatment of SAR, perennial allergic rhinitis, and chronic urticaria. It is a selective H_1-receptor antagonist[6] that has been shown to inhibit leukotriene[7] and prostaglandin production,[8] as well as ICAM-1 expression and eosinophil chemotaxis.[9]

In clinical studies, cetirizine has been compared with other oral second-generation antihistamines, including loratadine and fexofenadine. In two 2-day, placebo-controlled studies in an environmental exposure unit[10,11] and in a 2-day outdoor study,[12] cetirizine 10 mg once daily was more effective than loratadine in improving nasal symptoms in patients with SAR ($P \leq 0.05$). In two 2-week, multicenter studies comparing cetirizine 10 mg once daily with fexofenadine 120 and 180 mg once daily, there were no significant differences in efficacy between cetirizine and the 2 fexofenadine doses.[13,14] However, in another environmental exposure unit study,[15] cetirizine was significantly more effective than fexofenadine during the 24-hour interval after initial administration ($P < 0.001$).

Comparative studies of azelastine nasal spray have been carried out in Europe at a dosage of 1 spray per nostril twice daily, one half the recommended adult dosage in the United States. In a 2-week, double-blind study of azelastine nasal spray and intranasal beclomethasone in patients with SAR,[16] both treatments significantly improved symptom scores compared with placebo ($P < 0.001$), and there were no significant differences between treatment groups. In a 2-week, double-blind study in patients with SAR, azelastine nasal spray and cetirizine decreased nasal symptom scores by 60% and 63%, respectively, with no significant differences between treatments.[17] In addition, the results of placebo-controlled studies have indicated that azelastine nasal spray at a dosage of 2 sprays per nostril twice daily was effective in patients who remained symptomatic after treatment with loratadine[18] or fexofenadine.[19]

Given the preceding findings, the objective of the present study was to directly compare the efficacy and tolerability of azelastine nasal spray administered at the US recommended dosage of 2 sprays per nostril twice daily with those of cetirizine in the treatment of moderate to severe SAR.

PATIENTS AND METHODS

This was a randomized, double-blind, parallel-group, 2-week comparative trial conducted during the 2004 fall allergy season at 20 investigational research centers distributed throughout the major geographic regions of the United States.

Inclusion and Exclusion Criteria

Study investigators selected patients from their practices and/or recruited volunteers to participate in the study. Eligible patients were male and female patients aged ≥12 years with at least a 2-year history of SAR and a documented positive allergy skin test, either intradermal or epicutaneous, during the previous year. Patients were excluded for the following reasons: use of concomitant medication(s) that could affect the assessment of efficacy of study treatment; any medical or surgical condition that could affect the metabolism of study medications; clinically significant nasal disease (other than SAR) or significant nasal structural abnormalities; respiratory infection or other infection requiring antibiotic therapy within 2 weeks of the single-blind placebo lead-in period; past or current alcohol or drug abuse; and significant pulmonary disease, including persistent asthma requiring use of controller medication. Women of childbearing potential not using an accepted method of contraception and women who were pregnant or nursing also were excluded.

Study Design

This was a randomized, double-blind, parallel-group clinical trial designed to be consistent with a draft guidance from the US Food and Drug Administration for the conduct of clinical trials in allergic rhinitis.[20] A computer-generated randomization schedule was used to assign eligible patients to the 2 treatment groups in blocks of 4. The randomization schedule was provided by a biostatistical group employed by the sponsor, and access to the code was confidential and accessible only to authorized persons not involved in the study.

*Trademark: Zyrtec® (Pfizer Inc., New York, New York).

Blinding of the study was preserved at each study site until all patients had completed the study and the database was locked.

The study began with a 1-week, single-blind lead-in period, before which all previous allergy medications were discontinued (oral antihistamines for a minimum of 5 days and intranasal steroids for a minimum of 14 days before the start of the period) and patients received placebo nasal spray and placebo capsules. Patients qualified for entry into the lead-in period if they had a total nasal symptom score (TNSS) of ≥8 and a nasal congestion score ≥2 over the previous 12 hours (12-hour reflective TNSS).[20] The TNSS is a combined measure of the severity of nasal itching, nasal congestion, runny nose, and sneezing, each rated twice daily (morning and evening) on a 4-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe), with a maximum daily score of 24. Patients recorded their morning and evening 12-hour reflective symptom severity scores on diary cards for use by the investigator in determining their eligibility to enter the double-blind treatment period.

To be eligible for entry into the double-blind treatment period, patients must have recorded a morning or evening TNSS ≥8 on at least 3 days during the lead-in period and a morning or evening nasal congestion score of 3 on at least 3 days. For both the TNSS and nasal congestion score, 1 of the 3 pertinent days must have occurred within 2 days of the first day of the double-blind treatment period. In addition, because of the onset-of-action assessment (described in the following section), patients were required to have a TNSS ≥8 on the morning of randomization; patients who were not sufficiently symptomatic at that time were asked to return the next day for the onset-of-action assessment. Patients who did not meet the minimum symptom severity score at this time were not eligible for randomization. Patients who continued to meet the study inclusion criteria and met the minimum TNSS and nasal congestion criteria were randomized to receive treatment with azelastine nasal spray 2 sprays per nostril twice daily (morning and evening) plus placebo tablets (morning) or cetirizine 10-mg tablets once daily (morning) plus placebo saline nasal spray 2 sprays per nostril twice daily (morning and evening) for 2 weeks (days 1–14).

Azelastine nasal spray and placebo nasal spray were supplied by the manufacturer in spray-pump bottles of identical appearance. The placebo spray, which consisted of benzalkonium chloride, edetate disodium, hydroxypropyl methylcellulose, citric acid, dibasic sodium phosphate, and sodium chloride in purified water at pH 6.8 ± 0.3, was identical to the vehicle formulation contained in azelastine nasal spray. To mask their identity, the cetirizine 10-mg tablets were encapsulated in gelatin capsules size DB#C and overfilled with lactose. Placebo capsules were filled only with lactose. The dissolution rates of the cetirizine 10-mg tablets and encapsulated cetirizine 10-mg tablets overfilled with lactose were shown to be essentially identical at the 20- and 30-minute (100% dissolution) time points at 37°C in a comparative dissolution assay performed by McKesson Bioservices, Rockville, Maryland (MedPointe Pharmaceuticals, data on file). A placebo control group was not used in this study because both azelastine nasal spray and cetirizine have been shown to be safe and effective for the treatment of SAR.

The study was approved by Sterling Institutional Review Board, Atlanta, Georgia. All patients or their guardians (if aged <18 years) signed the approved informed consent agreement before participation.

Efficacy and Safety Variables

The coprimary efficacy variables were change from baseline to day 14 in the severity of rhinitis symptoms based on the combined morning and evening 12-hour reflective TNSS, and onset of action, based on the change from baseline in the instantaneous TNSS recorded in the physician's office immediately before the first dose of study medication and at 30, 45, 60, 90, 120, 150, 180, 210, and 240 minutes thereafter. Secondary efficacy variables were the change in TNSS from baseline to day 2 (end of the 24-hour dosing interval), and the change from baseline to day 14 in quality-of-life parameters for patients aged ≥18 years, measured using the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ).[21] The RQLQ assesses the domains of activities, sleep, nonnose/noneye symptoms, practical problems, nasal symptoms, eye symptoms, and emotions.

Tolerability was assessed in terms of reported adverse experiences and vital signs, which included body temperature, systolic and diastolic blood pressure, and heart and respiration rates, which were measured at baseline and at the end of the study.

Statistical Procedures

This study was designed to detect differences in TNSS and onset of action between the 2 active-treatment

groups. The sample size was based on the results of a double-blind, placebo-controlled pilot study in which 60 patients received 1 week of treatment with azelastine nasal spray, fluticasone nasal spray, cetirizine tablets, or placebo.[22] In this pilot study, an improvement in TNSS of 19.5% was observed with azelastine nasal spray, compared with 15.5% with cetirizine. A TNSS effect size of 0.25 (azelastine mean – cetirizine mean [pooled SD]) was identified for the change from baseline to the end of treatment using the same 4-point rating scale as in the present study. Based on this pilot study, it was estimated that ~150 patients per group would be sufficient to detect a difference in effect size of 0.25 between azelastine nasal spray and cetirizine for the primary efficacy variables with 80% power at the 0.05 level of significance.

The primary analysis was an intent-to-treat analysis that included all randomized patients with ≥1 postbaseline TNSS assessment. Missing TNSS values in this population were imputed using the last-observation-carried-forward method. The safety analysis included all randomized patients who received ≥1 dose of study medication and had ≥1 safety assessment after drug administration.

For the first primary efficacy variable (change in TNSS from baseline to day 14), the baseline score was calculated as the mean of the combined morning and evening TNSS during the placebo lead-in period. The change from baseline to day 14 was determined by subtracting the mean baseline score from the mean TNSS for the entire 2-week treatment period. Within-group comparisons were conducted using a paired *t* test, and between-group comparisons were conducted using an analysis-of-variance (ANOVA) model. The change from baseline in individual symptom severity scores was evaluated using a similar ANOVA model.

The second primary efficacy variable (onset of action) was determined based on the instantaneous TNSS over 4 hours. Within each treatment group, time to onset was determined using a paired *t* test on the change in TNSS from baseline. Between-group comparisons were made using the same ANOVA model as was used for change in TNSS from baseline to day 14.

The change in TNSS from baseline was also calculated for each day of the study. In assessing efficacy during the initial 24-hour treatment interval, the change in TNSS from baseline to day 2 was calculated based on the morning assessment on day 2, with baseline defined as the mean of the combined morning and evening TNSS during the lead-in period. Within- and between-group comparisons were performed using a paired *t* test and ANOVA, respectively.

Changes from baseline to day 14 in the individual RQLQ domains and the overall RQLQ score were calculated and analyzed according to the method described by Juniper at al.[21] Changes in vital signs were evaluated by comparing values before and after treatment.

All tests of significance were 2-sided. Baseline demographic and clinical characteristics were summarized descriptively.

RESULTS

Patient Disposition and Demographic Characteristics

Three hundred seven patients were randomized to receive double-blind treatment, and 299 patients completed 2 weeks of treatment (**Figure 1**). Data for all 307 patients were included in the safety assessment, and data for 306 patients were analyzed for efficacy (1 patient in the azelastine nasal spray group had no postbaseline diary data and was not included). Four patients in the azelastine group and 2 in the cetirizine group discontinued the study due to an adverse event, and 1 patient in each group was discontinued because of a protocol violation. The treatment groups were comparable in terms of demographic characteristics (**Table I**). Patients ranged in age from 12 to 74 years (mean, 35 years); 62.9% were female and 69.6% were white.

Efficacy Analyses

Change in TNSS from Baseline

During 2 weeks of treatment, both azelastine nasal spray and cetirizine significantly improved the combined morning and evening 12-hour reflective TNSS compared with baseline ($P < 0.001$). At the end of the study period, the mean improvement in TNSS was 5.56 (29.3% improvement) with azelastine nasal spray and 4.32 (23.0% improvement) with cetirizine. The overall difference in TNSS between the 2 groups across both weeks of the study significantly favored azelastine nasal spray ($P = 0.015$) (**Table II**). The improvement in daily symptom scores was significant for azelastine nasal spray compared with cetirizine on study days 8, 9, 10, 12, 13, and 14 (all, $P < 0.05$) (**Figure 2**). A per-protocol analysis that included 145 patients in the azelastine nasal spray group and 148 in the cetirizine group for whom complete data were

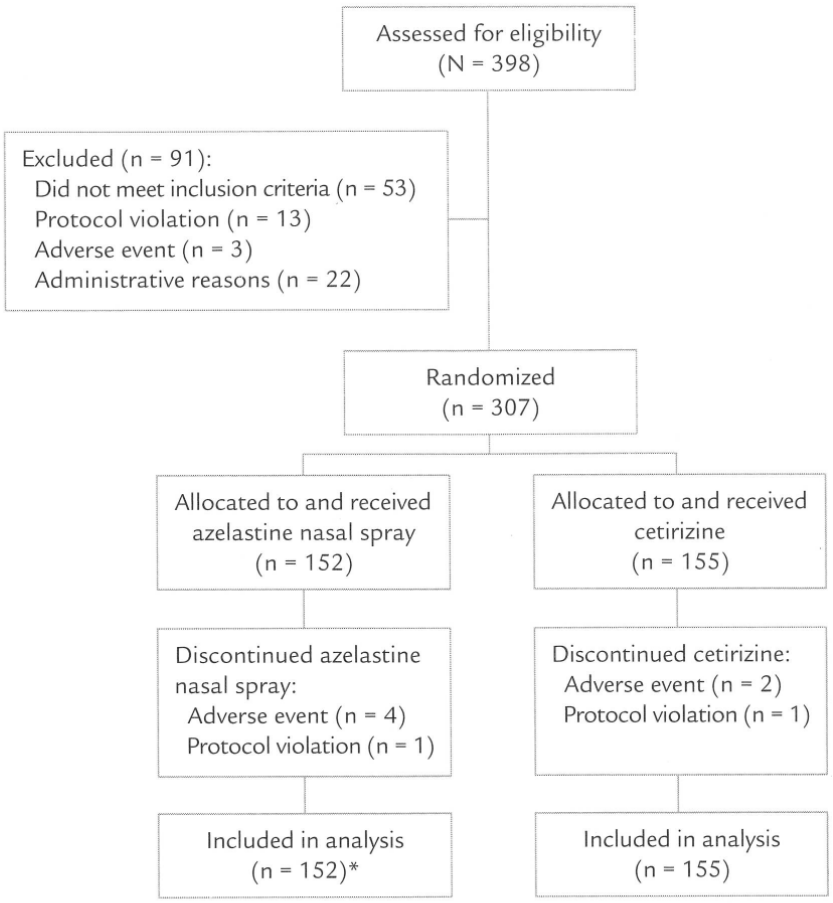

Figure 1. Patient disposition. *One patient had no postbaseline diary data and was not included in the efficacy analysis. All patients were included in the safety/tolerability analysis.

available also showed a significant difference in overall improvement in TNSS with azelastine nasal spray compared with cetirizine ($P = 0.023$).

All individual symptoms on the TNSS were significantly improved from baseline over the 2-week study period with both treatments ($P < 0.001$). There was a statistically significant improvement in runny nose with azelastine nasal spray compared with cetirizine ($P = 0.003$) (**Table II**).

Onset of Action

In the assessment of onset of action over 4 hours, the instantaneous TNSS was significantly improved from baseline in both treatment groups 15 minutes after initial administration ($P < 0.001$). The difference between treatment groups significantly favored azelastine at 60 and 240 minutes (both, $P = 0.040$) (**Figure 3**). At no time point during the 4-hour observation period did the improvement in TNSS with cetirizine exceed that with azelastine nasal spray.

Rhinitis Quality of Life Questionnaire

Scores on all individual domains of the RQLQ and the overall RQLQ score were significantly improved from baseline in both treatment groups (all, $P < 0.001$) (**Table III**). There were no statistically significant differences between azelastine nasal spray and cetirizine on any of the individual RQLQ domains. However, the overall difference was significant for azelastine nasal spray compared with cetirizine ($P = 0.049$).

Safety Profile

Both azelastine nasal spray and cetirizine were well tolerated. The most common adverse events with azelastine nasal spray were bitter taste (3.3%), headache (2.6%), epistaxis (2.0%), somnolence (1.3%), and nasal

Table I. Demographic characteristics of study patients.

Characteristic	Azelastine Nasal Spray (n = 152)	Cetirizine (n = 155)
Sex, no. (%)		
Female	96 (63.2)	94 (60.6)
Male	56 (36.8)	61 (39.4)
Age, y		
Mean	35.6	35.7
Range	12–74	12–74
Race, no. (%)*		
White	107 (70.4)	107 (69.0)
Black	29 (19.1)	30 (19.4)
Asian	3 (2.0)	6 (3.9)
Other	13 (8.6)	12 (7.7)
Duration of SAR, y		
Mean	18.8	20.0
Range	2–51	2–58

SAR = seasonal allergic rhinitis.
*Percentages may not equal 100 due to rounding.

discomfort (1.3%). The most common adverse event with cetirizine was somnolence (2.6%). All other adverse events were reported in <1% of patients. Four patients in the azelastine group discontinued the study due to adverse events (1 each, sleeplessness, sinus infection, nausea, and allergy exacerbation). One patient in the cetirizine group discontinued the study due to somnolence and 1 discontinued due to a skin rash. No clinically significant abnormalities in vital signs were noted during the study.

DISCUSSION

It is often asked whether there are clinically important differences between the antihistamines available for the treatment of allergic rhinitis. Both intranasal and oral second-generation antihistamines are recommended as first-line therapy for allergic rhinitis[23]; however, earlier well-controlled comparative clinical trials of 2 weeks of treatment with oral second-generation antihistamines have primarily shown similarities among them.[13,14] Although azelastine nasal spray significantly improved symptoms in patients who remained symptomatic after treatment with oral loratadine[18] or fexofenadine[19] compared with placebo ($P \leq 0.007$), these studies did not directly compare active-treatment groups. The present study, therefore, was designed with a sufficient sample size to detect significant differences in the selected efficacy parameters between azelastine nasal spray and cetirizine. The investigational sites were distributed throughout the major geographic regions of the United States to ensure that the study population included a representative sample of patients with symptoms of SAR caused by a broad spectrum of seasonal allergens.

During the 2-week treatment period, azelastine nasal spray significantly improved the overall TNSS compared with cetirizine in patients with moderate to severe SAR ($P = 0.015$). Azelastine nasal spray also improved scores for all 4 individual symptoms included in the TNSS, with significantly greater improvement in runny nose compared with cetirizine ($P = 0.003$). The difference in TNSS between azelastine nasal spray and cetirizine became more evident as the study progressed, with significant differences in TNSS with azelastine nasal spray compared with cetirizine on study days 8, 9, 10, 12, 13, and 14 (all, $P < 0.05$).

In the assessment of onset of action, both treatment groups had significant improvements from baseline at 15 minutes (the first time point) after the initial administration of medication and at each subsequent time point in the 4-hour assessment period ($P < 0.001$). Based on a comparative study of cetirizine and fexofenadine that showed no significant improvement in symptoms with cetirizine compared with placebo during the first 2 hours after initial administration,[24] the early onset of activity in the cetirizine group in the present study may be attributable to the effect of the saline nasal spray vehicle. There was a significant difference with azelastine nasal spray compared with cetirizine at 60 minutes after initial administration of medication and at the last assessment time (240 minutes) (both, $P = 0.040$), which is consistent with the peak effect observed with azelastine nasal spray in placebo-controlled studies assessing onset and duration of action.[25,26]

Patient-reported symptom assessments are the fundamental method for evaluating efficacy in allergy clinical trials.[20] However, in the majority of patients with rhinitis, particularly those with SAR, improving well-being and quality of life should be among the primary goals of treatment.[27] In this study, scores on the individual RQLQ domains and the overall RQLQ score were significantly improved from baseline in

Table II. Least squares (LS) mean change and percentage change from baseline in the total nasal symptom score (TNSS) and individual symptom scores* (n = 151 azelastine nasal spray† and n = 155 cetirizine). The treatment groups were comparable at baseline in terms of the TNSS and all individual symptoms.

Symptom/ Treatment Group	Baseline, LS Mean (SD)‡	LS Mean (SD) Change from Baseline‡	% Change	*P* vs Baseline§	*P* vs Cetirizine‡
TNSS					
Azelastine nasal spray	18.82 (2.86)	5.56 (4.68)	29.3	<0.001	0.015
Cetirizine	18.50 (2.85)	4.32 (4.66)	23.0	<0.001	
Itchy nose					
Azelastine nasal spray	4.63 (1.14)	1.39 (1.45)	29.5	<0.001	0.056
Cetirizine	4.64 (0.98)	1.09 (1.46)	21.7	<0.001	
Nasal congestion					
Azelastine nasal spray	5.31 (0.62)	1.13 (1.16)	21.1	<0.001	0.187
Cetirizine	5.27 (0.62)	0.96 (1.26)	18.1	<0.001	
Runny nose					
Azelastine nasal spray	4.74 (0.97)	1.46 (1.39)	29.8	<0.001	0.003
Cetirizine	4.61 (0.95)	1.00 (1.40)	19.6	<0.001	
Sneezing					
Azelastine nasal spray	4.14 (1.25)	1.58 (1.49)	33.8	<0.001	0.065
Cetirizine	3.98 (1.32)	1.29 (1.36)	28.2	<0.001	

*The TNSS is a combined measure of scores for the severity of itchy nose, nasal congestion, runny nose, and sneezing, rated twice daily (morning and evening) on a 4-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe), with a maximum daily score of 24.
†One patient had no postbaseline diary data and was not included in the efficacy analysis.
‡Analysis-of-variance model.
§Paired *t* test.

both treatment groups (all, $P < 0.001$); however, the improvement in overall score was significantly greater with azelastine nasal spray compared with cetirizine ($P = 0.049$). Improvements in the symptom-related domains of the RQLQ were consistent with the improvements in TNSS, and these symptom-related improvements were accompanied by improvements in quality-of-life domains relating to function, including activities, sleep, practical problems, and emotions.

The design of the study did not include a placebo control group, as both azelastine nasal spray and cetirizine are proven therapeutic modalities. To maintain double-blinding, a double-dummy technique was used in which each patient received either an identity-concealed bottle of azelastine nasal spray plus placebo capsules, or encapsulated cetirizine tablets plus placebo saline nasal spray. The placebo saline nasal spray was the same vehicle formulation contained in azelastine nasal spray. The positive effect of saline nasal spray on allergic mediators and symptoms has been reported in clinical trials in patients with allergic rhinitis[28,29]; therefore, patients randomized to receive cetirizine were also receiving an "active placebo." The use of an active placebo in the cetirizine group may have reduced the difference between the 2 treatment groups; in actual practice, where a saline nasal spray is not generally used along with an oral antihistamine, the difference in effect between azelastine nasal spray and cetirizine may be greater than was observed in this study. In a previous multicenter study,[17] azelastine nasal spray at a dosage of 1 spray per nostril twice daily and cetirizine 10 mg once daily were equally effective after 14 days of treatment. Use of the US recommended dosage of 2 sprays per nostril twice daily may have contributed to the increased effectiveness seen with azelastine nasal spray in the present trial.

CONCLUSIONS

In this study conducted during the fall allergy season in patients with moderate to severe SAR, azelastine nasal

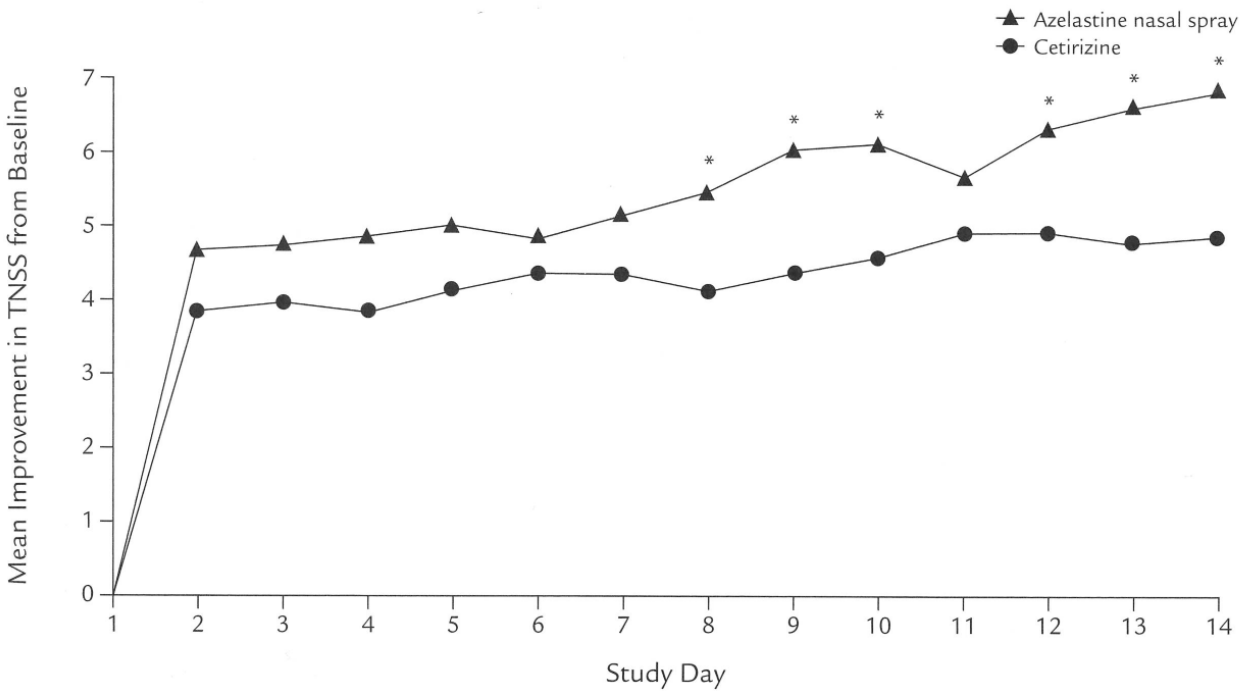

Figure 2. Mean improvement from baseline to day 14 in combined morning and evening 12-hour reflective total nasal symptom score (TNSS). Both treatments produced significant improvements from baseline ($P < 0.001$). The improvement over 14 study days was significant for azelastine nasal spray compared with cetirizine ($P = 0.015$). *$P < 0.05$ versus cetirizine.

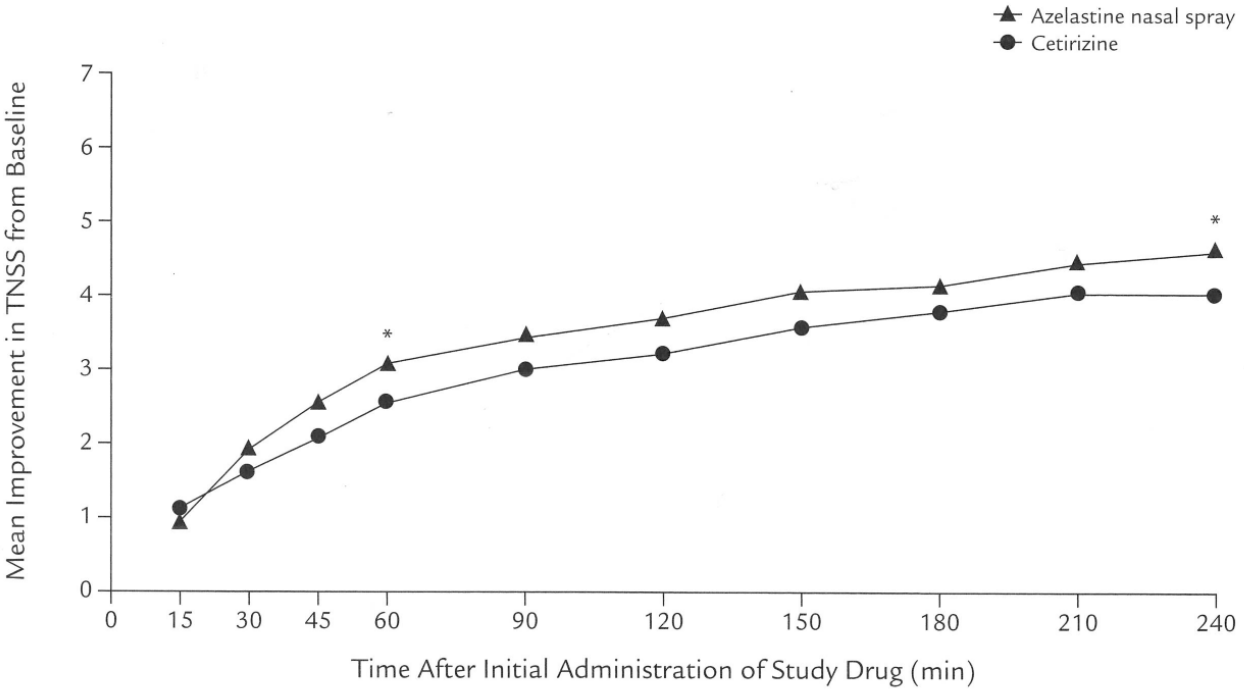

Figure 3. Onset of action over 4 hours after the initial administration of study drug. Both treatments produced significant improvements from baseline in instantaneous total nasal symptom score (TNSS) 15 minutes after initial administration ($P < 0.001$). *$P = 0.040$ versus cetirizine.

Table III. Least squares (LS) mean change in Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores in patients aged ≥18 years. The treatment groups were comparable at baseline on all domains of the RQLQ.

RQLQ Score/ Treatment Group	Baseline, LS Mean (SD)*	LS Mean (SD) Change from Baseline*	*P* vs Baseline†	*P* vs Cetirizine*
Overall				
Azelastine nasal spray	3.69 (1.04)	1.41 (1.25)	<0.001	0.049
Cetirizine	3.75 (1.03)	1.11 (1.18)	<0.001	
Activities				
Azelastine nasal spray	4.41 (1.05)	1.57 (1.52)	<0.001	0.110
Cetirizine	4.46 (1.05)	1.28 (1.43)	<0.001	
Sleep				
Azelastine nasal spray	3.48 (1.43)	1.18 (1.32)	<0.001	0.729
Cetirizine	3.40 (1.44)	1.12 (1.52)	<0.001	
Nonnose/noneye symptoms				
Azelastine nasal spray	3.33 (1.35)	1.18 (1.36)	<0.001	0.123
Cetirizine	3.43 (1.21)	0.92 (1.36)	<0.001	
Practical problems				
Azelastine nasal spray	4.15 (1.28)	1.61 (1.51)	<0.001	0.134
Cetirizine	4.23 (1.29)	1.33 (1.51)	<0.001	
Nasal symptoms				
Azelastine nasal spray	4.29 (1.04)	1.60 (1.44)	<0.001	0.072
Cetirizine	4.35 (1.21)	1.28 (1.54)	<0.001	
Eye symptoms				
Azelastine nasal spray	3.62 (1.44)	1.49 (1.59)	<0.001	0.251
Cetirizine	3.62 (1.55)	1.26 (1.65)	<0.001	
Emotions				
Azelastine nasal spray	3.22 (1.40)	1.22 (1.48)	<0.001	0.461
Cetirizine	3.26 (1.38)	1.09 (1.45)	<0.001	

*Analysis-of-variance model.
†Paired *t* test.

spray was well tolerated and produced significantly greater improvements in TNSS and total RQLQ score compared with cetirizine over 2 weeks of treatment. In the assessment of onset of action, azelastine nasal spray provided significantly greater symptom relief compared with cetirizine at 60 minutes after the initial dose and at the end of the 4-hour observation period.

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